CHAPTER - 2

PACKAGING MATERIALS

Points to be covered in this topic

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PACKAGING MATERIALS

2.1 INTRODUCTION

- Packaging is an **art**, **science** and **technology** which deals with the study of materials and methods used to pack the product; and also, the knowledge of the machinery used for packing the product.
- Packaging container **may or may not be in direct contact** with the product.
- The **basic purpose of packaging** is to protect the integrity, purity, potency and quality of the product.

❖ Objectives of packaging

The objectives of packaging are

- **To protect the product** from damage during transport.
- **To preserve the product** until it is opened for use by the consumer.
- **To contain small parts** so they will not be lost before assembly.
- **To help sell or market** the product with name, brand, and product information.

❖ Advantages of packaging

- Packaging helps the product to **reach consumer in economic way** with proper storage.
- It **maintains the stability** of the products.
- It **allows proper labelling** of the product which makes it easier to identify.
- It provides hygiene.
- It **decreases the product cost** by packaging in small quantities.

2.1.1Components of packaging

1. **Container** is a device that holds the drug and it may or may not be the in direct contact with the pharmaceutical preparations.

2. **Closure** is the device by means of which container can be open and closed.

3. **Liner** is the material which is inserted in a cap.

4. **Carton** is the out covering which gives secondary protection against mechanical and environment hazards.

5. **Box** is the device used for packaging multiples of the products.

2.1.2Classification of Pharmaceutical Packaging

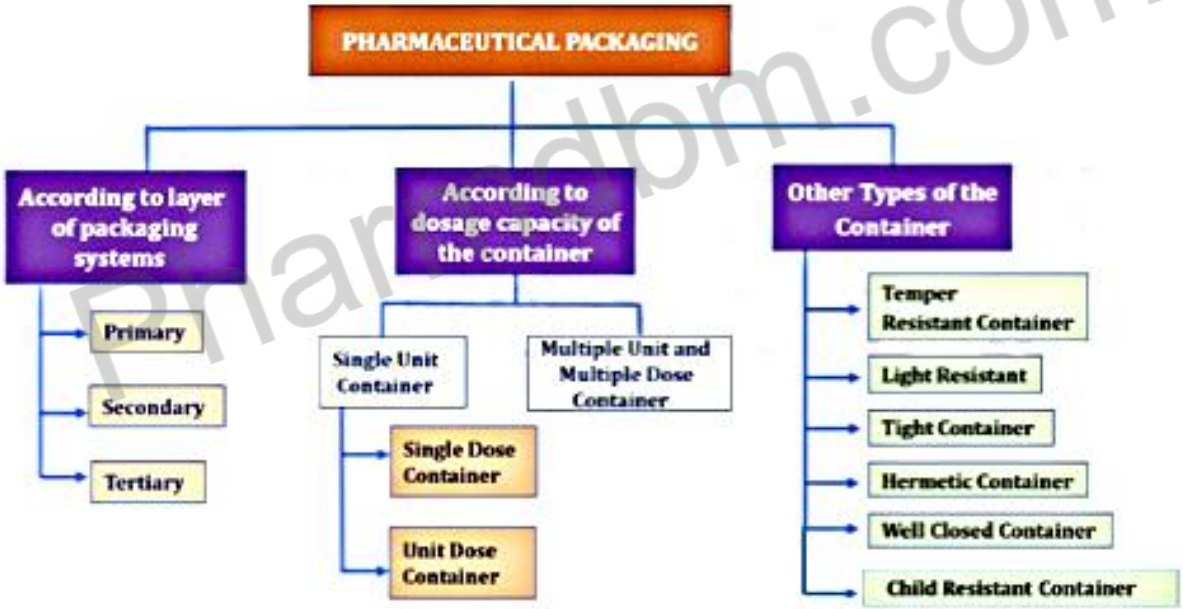

Fig 2.1: Classification of Pharmaceutical Packaging

1. According to layer of packaging system

Fig 2.2: Types of packaging according to layer of packaging system

i. Primary Packaging

- Primary Packaging is the material that **first envelops** the product and holds it.
- This is the **smallest unit of distribution** and is the package which is in the **direct contact with the product.**
- The packaging needs to be such that there are **no interactions with the drug** and will provide proper containments of the pharmaceuticals.
- **Function - Restrict** the any chemical, climatic or biological or occasionally mechanical hazards that may cause or lead product deterioration.
- **Examples:** Blister Packages, Strip Packages, Ampoules, Vials, glass and plastic bottles etc.

ii. Secondary Packaging

- Secondary Packaging is **outside the primary packaging** and used to group primary packages together.
- The secondary packaging mainly **provides the additional protection** necessary to endure the safe warehousing and for refill packaging.
- **Examples:** Boxes, leaflets, shrink wraps etc.

iii. Tertiary Packaging

- Tertiary Packaging is **used for bulk handling,** warehousing storage and transported shipping. The most common form is a palletized unit load that packs tightly into the containers.
- It is used to **not only protect the product but also its primary and secondary packaging.**
- **Examples:** Cardboard Containers, Barrels, crates, edge protectors etc.

2. According to dosage capacity of the container

i. Single Unit Container

- **Single Unit container** is may be defined as a container whose contents are to be used immediately after opening or a container designed to hold the quantity of the drug product that is to be administered as a single dose.

a) Single Dose Container

- A single dose container holds a quantity of preparation intended for total or partial use as a single administration. It is mainly used for parenteral products.

b) Unit Dose Container

- A Unit dose container is meant for drug that are to be administered as a single dose by a route other than the parented route directly from the container.

ii. Multiple Unit Container and multiple dose container

- Multiple Unit Container and multiple dose container allows multiple withdrawal of a portion of the content without effecting the strength, quality or purity of the remaining content.

3. Other types of the container

i. Temper Resistant Container

- According to FDA, Tamper Resistant Packaging is one having an indicator or barrier to entry which is breached or missing can reasonably be expected to provide visible evidence to consumers that tampering has occurred.

✓ Types of Temper Resistant Packaging

- There are various types of Temper Resistant Packaging as given in Table 2.1

Table 2.1: Types of Temper Resistant Packaging

TYPES	DESCRIPTION
✓ **Film Wrapping** 	• Film wrapping has been used extensively over the years for **products requiring package integrity** or **environmental protection**. • It can be generally categorized into the following types: a. End-folded wrapper, b. Fin seal wrapper, Shrink wrapper

✓**Blister Packaging** 	• Blister packaging is a type of packaging **produced by heating a sheet of plastic** and **moulding it into shape** to form a bubble or pocket the 'blister' that completely covers the product.
✓**Strip Packaging** 	• A strip package is formed by **feeding two webs of a heat-sealable flexible film** through either a heated crimping roller or a heated reciprocating plate.
✓**Shrink Banding** 	• Shrink bands are pieces of plastic casing that **wrap around bottles** and jars to prevent tampering. • The heat-shrinkable polymer is manufactured as an extruded, oriented tube in a diameter slightly larger than the cap and neck ring of the bottle to be sealed.
✓**Bottle Seals** 	• A bottle may be made **tamper-resistant** by bonding an inner seal to the rim of the bottle in such a way that **access to the product** can only be attained by irreparably destroying the seal.
✓**Tape Seals** 	• Tape sealing **involves the application of a glued** or **pressure-sensitive tape** or label around or over closure of package, which must be destroyed to gain access to the packaged product.
✓**Breakable Caps** 	• Breakable closures come in different designs. • The roll-on cap design **used in the past for carbonated beverages** uses an aluminum shell, which is placed over the bottle neck during the capping operation. • This lower portion of the cap blank is usually perforated so that it breaks away when cap is unscrewed, which **serves as visible sign of prior opening.**
✓**Sealed Tubes** 	• **Sealed tubes** used for packaging are made up of metal, plastic, or lamination of foil, paper, & plastic.

ii . Light Resistant Packaging

- **Light Resistant Containers** are used to protect the medicaments from harmful effects of light.
- Light sensitive products **can be protected** by storing the clear, transparent and translucent container in a dark place.

Examples: Amber glass, red glass etc.

iii. Tight Container

- A **Tightly Closed Container** protects the medicaments from contamination with any liquids, solid or vapors or from loss or deterioration of the drug product **due to effervescence, deliquescence** or **evaporation** under the normal conditions.

Examples: Cartoons, crates etc.

iv. Hermetic Container

- Hermetically Sealed Containers are those containers that **does not allow the air** and **other gases to pass through either direction under normal** condition of handling, shipment, storage and distribution.
- These contains single dose only.

Examples: Aluminum cans, metal foils and gas impermeable plastics.

v. Well Closed Container

Well Closed Containers are those which **protects the contents from loss** and from **contamination with the dust** or other particles present in the environment under the normal condition of handling, shipment, storage, and distribution.

Examples: Ampoules

vi. Child Resistant Container

Child Resistant Packaging also referred to as **"special packaging"** reduce the risk of poisoning in children via **the ingestion of potentially hazardous items** including certain prescription and over-the-counter (OTC) medications, pesticides, and household chemicals.

2.2 SELECTION CRITERIA FOR PACKAGING MATERIALS

Selection of containers requires a careful consideration of the following points:

1. **Physical characteristics** – Packaging material selection decisions are influenced by certain **physical characteristics of the product** like the physical state, weight, stability, rigidity to be packaged.

2. **Sterility of the product** - It is necessary to use hermetic or airtight containers. For injectable, hermetic containers are used and for other preparations air tight containers are used.

3. **Light Sensitivity of Medicament** - For light sensitive drugs, light resistant containers such as **amber glass containers** or **black thermoplastic containers**. The black paper protects the product from the harmful effects of light.

4. **Volatility of medicament and other ingredients** - If the product contains a volatile substance or if the preparation is volatile in nature, an air tight container to **prevent the evaporation of the volatile substance.**

5. **Pressure inside the container** - If the pressure inside the container remains higher than the atmospheric pressure as in case of aerosols, a mechanically strong container should be used.

6. **Incompatibility between the constituents of the product and the container** - Some medicaments like **alkaline liquids** have the capacity to extract out alkali from glass containers.

- The extracted alkali can **deteriorate the product** and it can be incompatible with the constituents of the product. So, for these types of preparations, only those containers which comply with the limit test of alkalinity of glass should be used.

- Some medicaments can **extract out lead** or **arsenic** from glass containers. For these preparations lead or arsenic free glass containers should be used.

7. **Hygroscopic properties of the preparation or medicament** - If the preparation is **hygroscopic in nature**, an air tight container should be used.

8. **Stability** – Many **environmental factors** like moisture, oxygen, light, flame and chemical reaction affect stability of formulation. So. Stability of the product should be major concern.

9. **Formulation components** – The product may react with the packages such as **release of alkali** from the glass is destabilized. Thus, stability and compatibility with the formulation contents is necessary.

10. **Regulations** – Packaging should be done according to the government regulation in countries **to avoid any kind of substandard package**.

Table 2.2: Type of container used for specific medicaments

MEDICAMENT	TYPE OF CONTAINER USED
Eye and ear drops	Dropping bottles
Ointments and creams	Collapsible tubes or wide mouth bottles
Ointments applied in the rectum or other body cavities like nose	Collapsible tubes with nozzles
Capsules and tablets	Strips or in bottles
Injectable	Vials and ampoules
I/V fluid	I/V fluid bottles or thermoplastic bags

2.3 TYPES OF PACKAGING MATERIAL

Fig 2.3: Types of Packaging Materials

2.3.1 Glass Containers

- Glass is the most commonly used material for construction of a container for a wide variety of pharmaceutical preparations.
- It is **made up of heating mixture of** silica (59-80%), sodium oxide (12-17%), calcium oxide (5-12%) aluminium oxide (0.5-3.0%), cullet and additives such as oxides of potassium, magnesium, boron.

➢ Advantages

- Glass is transparent which **allows the visual inspection** of the contents.
- They are **economical** and easily available in various shapes and sizes.
- They are chemically inert, quite strong and rigid.
- It can be molded any shape.
- They possess **superior protection properties**.

➢ Disadvantages

- Glass is **fragile** in nature.
- It is heavy, that can **increase transportation charges**.
- It may **release alkali** to aqueous preparations.
- Glass packaging is **comparatively expensive**.

Process of Forming Glass Container

(1) Blowing: In this method **compressed air is used to form the molten glass** in the cavity of a mold.

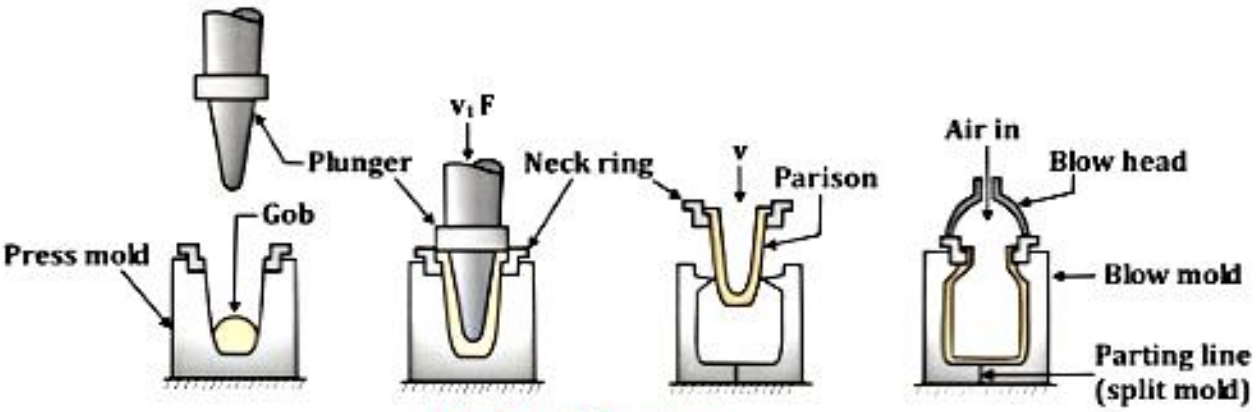

Fig 2.4: Blowing

(2) Drawing: It involves the **pulling of molten glass through dies** that shape the soft glass into ampoules, vials etc.

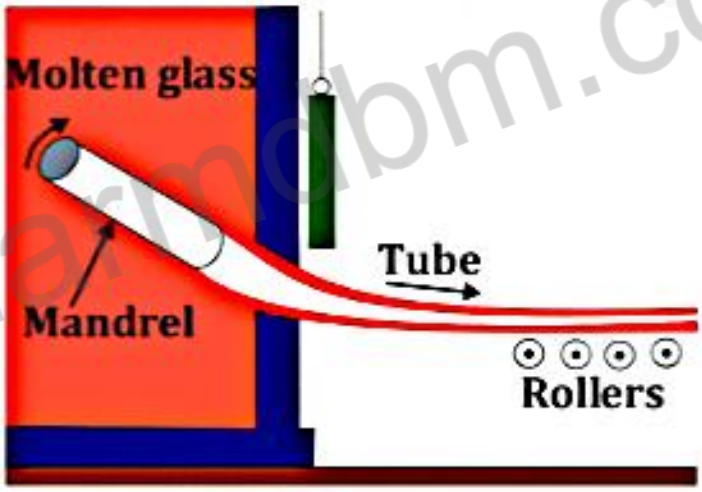

Fig 2.5: Drawing

(3)Pressing: In this method, glass containers are formed by **use of mechanical force** which presses the molten glass against the ride of a mold.

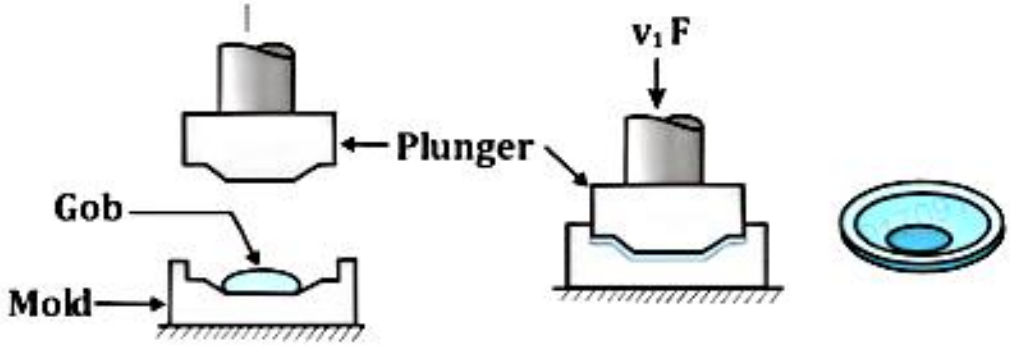

Fig 2.6: Pressing

(4) Casting: In this method, the **force of gravity** or **centrifugal force** is used to initiate the formation of molten glass in the cavity.

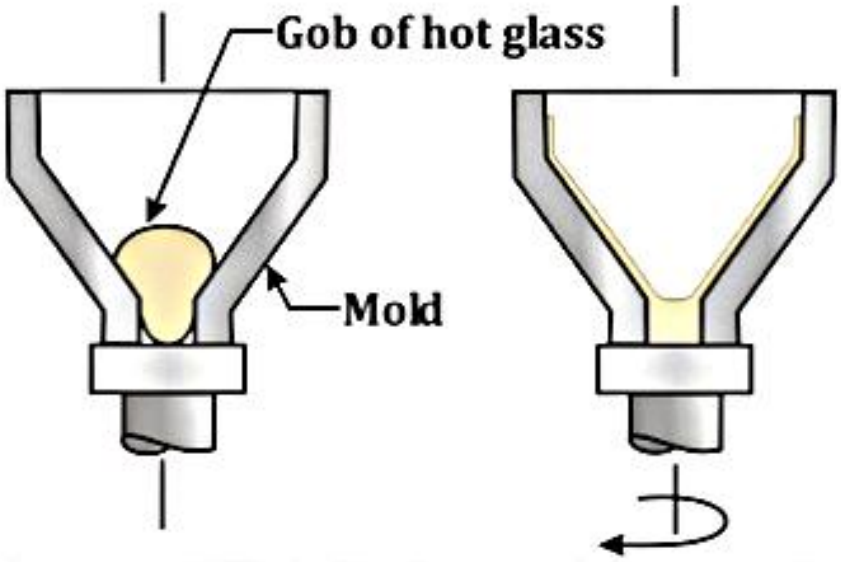

Fig 2.7: Casting

➢ Types of Glass Container

- There are mainly four types of glass container depends on various factor such as product, type of test and test limit as given in Table 2.4

Table 2.3: Types of Glass Container

TYPES OF GLASS	GENERAL DESCRIPTION	TYPE OF TEST	TEST LIMIT	
			Size (ml)	ml of 0.02N H_2SO_4
I	Highly heat resistant borosilicate glass	Powdered glass	All	1.0
II	Treated soda - lime glass	Water Attack	100 ml or less	0.7
			Over 100 ml	0.2
III	Soda -lime glass	Powdered glass	All	8.5
IV(NP)	General-purpose soda-lime glass	Powdered glass	All	15.0

✓ Type I / Borosilicate glass

- Borosilicate glass is a **highly resistant glass**, due to presence of boric acid.
- It contains 80% silica, 10% boric oxide, small amount of NaOH and aluminum oxide.
- It has **high melting point** and used to prepare laboratory glass apparatus.
- It is suitable for packaging material for **parenteral** or **non-parenteral** products.

✓ Type II / Treated soda lime glass

- Soda Lime Glass is a most simple form of glass **prepared from silica, soda-ash** and **limestone.**
- It is prepared by **treating inner surface of type III glass** with Sulphur.
- **Blooming** or **weathering** is a phenomenon that affects the appearance of glass containers, especially when they are exposed to humid or variable environmental conditions. It is caused by the dissolution of salts from the glass surface by condensed moisture, which then crystallize as the water evaporates.
- During manufacturing surface alkali is de-alkalized that **prevents weathering of empty glass** bottles.
- It can be used to **store alkali sensitive products.**

❖ Typical Compositions of Soda Lime Glass

Table 2.4: Composition of Soda lime glass

COMPOSITION	PERCENTAGE
Silicon-di-oxide	66-75%
Sodium oxide	12-19%
Calcium oxide	6-10%
Potassium oxide	Less than 1%
Magnesium oxide	Less than 1%
Aluminum oxide	Less than 1%

✓ **Type III / Regular Soda-lime Glass**

- **Regular soda lime containers** are untreated and made of commercial soda-lime glass.
- **It contains** 75% silica, 15% sodium oxide, 10% calcium oxide, small amount of aluminium oxide, magnesium oxide and potassium oxide.
- **Aluminium oxide** impacts chemical durability and magnesium oxide reduces temperature required during moulding.
- **Type III glass** is generally not used for parenteral preparations.

✓ **Type IV / NP—General-purpose Soda-lime Glass**

- **General purpose soda lime glass** containers made up of plain soda-lime.
- This type of glass is supplied for **non-parenteral products**.
- It is having **low hydrolytic resistance** and not used for products that need to be autoclaved as its surface erosion increases with temperature

➢ **Some other types of glass are**

1. **Silicone treated glass:** Glass is treated with silicone so that it can be used for preparing containers to store alkali sensitive products. Silicone is an excellent choice for heat-resistance applications.
2. **Sulphured glass:** It is a cheaper variety of glass used for the construction of containers for parenteral products.
3. **Neutral glass:** Neutral glass is a borosilicate glass containing significant amounts of boric oxide, Aluminium oxide, alkali metal oxides and/or alkaline earth oxides in the glass network.
4. **Amber colored glass:** Amber color glass is particularly useful when your product is light sensitive. Amber glass is actually a mixture of sand, limestone, and soda ash. Amber glass containers are created by adding carbon, iron, and sulphur into the raw material mixture. These materials provide the iconic color of amber glass – a rich amber color.

2.3.2 Plastic Containers

- Plastics are **synthetic polymers of high molecular weight**. Plastic is made from one or more polymers together with certain additives.
- The additives included in plastic formulation are antioxidants, antistatic agents, colors, lubricants, plasticizers and stabilizers.

➢ Advantages

- Plastics are available in various shapes and sizes.
- These offer a high flexibility; transportation cost is low.
- These are light in weight and can be handled easily.
- These are unbreakable and can be transported easily.

➢ Disadvantages

- Plastics are permeable to water vapors and atmospheric gases. They are non-biodegradable.
- They cannot withstand heat without softening or distorting.
- They may interact with certain chemical to cause softening or distortion.
- They may absorb chemical substances, such as preservatives for solution.
- These are having low melting point and hence cannot desired level of protection against heat.

➢ Types of Plastics

1. **Thermoplastic type** - Thermoplastic gets softened to a viscous fluid on heating and hardens again on cooling. The hardness after cooling is influenced by the degree of cross linkage or inter-molecular attraction between the long chain molecules e.g., nylon, polystyrene and polymethyl methacrylate.

2. **Thermosetting type - Thermosetting plastic** may become flexible but does not become fluid on heating.

- They are generally **hard and brittle at room temperature** because of a high degree of cross linking.
- E.g., phenol formaldehyde, Melamine formaldehyde and urea formaldehyde, Epoxy resins, polyurethanes.
- The polymers commonly used to make plastic container are as follows

i. Polyethylene: Polyethylene is available in **three different grades** namely low, medium and high density ranging from **0.91-0.96 g/ml.** It is impermeable to water vapors and does not deteriorate with age unless it is exposed to sunlight for a long period. It is used for preparing disposable syringes and containers for packaging of a number pharmaceutical preparations.

ii. Polyvinyl Chloride (PVC): Polyvinyl Chloride is less flexible. It is used for preparing eye-ointment tubes.

iii. Polymethyl Metho Acrylate (PMMA): Polymethyl Metho Acrylate is a hard, strong but light, transparent plastic. It is used for preparing bottles and tubes.

iv. Polystyrene: Polystyrene is a hard, rigid, light material. It can be easily molded into shape. So, it is used for preparing bottles, tubes, jars, boxes and syringes.

v. Polytetra fluoroethylene (PTFE): Polytetra fluoroethylene is translucent, opaque and possesses high any resistance to solvents and chemicals.

vi. Polycarbonate: The polycarbonate has **good impact resistance** and **stability.** It has low absorption capacity and is heat resistance. It is used for making reusable bottles, membrane filters and sterilizable medical packaging.

vii. Polyvinylidene chloride: Polyvinylidene chloride is **copolymer of vinyl chloride.** It has an excellent resistance to permeation by moisture and gas and used as coating.

viii. Polypropylene: Polypropylene is used for **blister packages.**

2.3.3 Metal Packaging

- A Metal Packaging is **most versatile** of all the materials and are strong, unbreakable, opaque substances.
- These are used in **packaging of non-parenteral products** due to particle shedding properties.
- Metal such as aluminum, tin plated steel, stainless steel, tin, and lead are used for production of containers as these are resistant to temperature variation.

➢ **Advantages**

- Metals are **impermeable to light**, moisture and gases.
- These are made into rigid unbreakable containers by impact extrusion.
- These are **light in weight compared** to glass containers.
- Labels can be printed on the surface.
- These are suitable for pressurized packaging.

➢ **Disadvantages**

- Metals are expensive.
- It reacts with certain chemicals or drugs.
- It shows chances of toxicity.

Table 2.5: Application of Metal as packaging Material

PACKAGE	DOSAGE FORM	REMARKS
Strip, blister	Tablet, capsules	Aluminium coated polymer used to improve sealability and stability
Collapsible tubes	Ointments, creams, gels	It has internal protective coating of polymer
Cans	Aerosols, inhalers, sprays	Pressure resistant and internal polymer coated aluminium containers are available

➢ **Types of metals**

✓ **Aluminum**

- **Aluminum creates a barrier** to protect the product from contaminations such as light, oxygen and moisture **ensuring longer shelf life** and **higher security** to patients.
- In foils, it is used at **99% purity** and above with a gauge thickness of 0.6-0.40 µm.

✓ **Tin**

- Tin containers are preferred for food, pharmaceuticals, or **any product for which purity** is of para-amount consideration.
- It is chemically inert of all **collapsible tube metals. Tin in 15%** in composition of metals is used for collapsible tubes.
- It is used for **production of aerosols** cans by electroplating in onto sheet steel to improve corrosion resistance and facilitate soldering.
- Laminates of tin coated lead are cheaper than tin alone. It is alloyed with about 0.5% copper for stiffening.

✓ **Lead**

- Lead has the **lowest cost of all-tube** metals. It is generally used for non-food products such as adhesives, lubricants, paints and inks.
- The **lead should never be used** for anything taken internally because of the risk of lead poisoning. With internal linings, lead tubes are used for such products as fluoride toothpaste.

2.3.4 Rubber Packaging

- Rubber consists of **long chain polymers** of isoprene units linked together. Rubber also containing, vulcanizing agent, activators, filters, softeners, antioxidants, pigments, lubricants and miscellaneous substances like paraffin wax, resins etc.
- The **ideal properties of rubber** include elasticity, hardness, tendency to fragment, resealability, vaccum retention, coring and break force.

Table 2.6: Classification of Rubber

CLASSIFICATION OF RUBBER	
Natural rubber	• Natural rubber is suitable for multiple use closures for injectable products as rubber reseals after multiple insertion of needle. • It consists of latex from *Hevea Brasiliensis* and is an isoprene polymer. Natural rubber can be converted into smoked sheet of pale crepe. • **Example:** Brasiliensis is a favoured source for commercial use.
Synthetic rubber	• Synthetic rubber is an artificial elastomer. • Synthetic rubber is silicone, neoprene, nitrile or butyl rubber. They are expensive. **Example:** Polychloroprene, Polybutadiene, Nitrile rubber.

➢ **Advantages**

- **Rubber** does not deteriorate with age.
- Good quality rubber is **resistant to sterilization** conditions.
- They are **unbreakable, tough** and can be easily transported.
- Rubber acts as self-seal to the containers.
- Although porous they do not allow the **transfer of water vapors** or gases in either direction.

➢ **Disadvantages**

- The **composition of rubber** stoppers is complex and the manufacture process is complicated.
- **Soft rubber** can be attached by oxidizing media, oils and organic solvents.
- **Hard rubber** may produce large number of fragments when the hypodermic needle cuts through the closure and the fragmented material may appear in the solution.